# WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Friday, February 01, 2008

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
| | *DB=PGPB,USPT; PLUR=YES; OP=ADJ* | | |
| ☐ | L16 | L15 and (514/37.icls. or 514/37.ccls. or 546/206.icls. or 546/206.ccls.) | 0 |
| ☐ | L15 | L14 and (@AD<20021213 or @PRAD<20021213 or @RLAD<20020213) | 18 |
| ☐ | L14 | L13 and (donepezil or aricept) | 50 |
| ☐ | L13 | severe adj3 (Alzheimer's) | 306 |
| ☐ | L12 | L10 and (514/37.icls. or 514/37.ccls. or 546/206.icls. or 546/206.ccls.) | 0 |
| ☐ | L11 | L10 and 514/37.icls. or 514/37.ccls. or 546/206.icls. or 546/206.ccls. | 884 |
| ☐ | L10 | L9 and (donepezil or aricept) | 303 |
| ☐ | L9 | L8 and (@AD<20021213 or @PRAD<20021213 or @RLAD<20020213) | 10037 |
| ☐ | L8 | (Alzheimer's) and (severe or MMSE or sMMSE or (mini-mental state)) | 14294 |
| ☐ | L7 | L6 and (donepezil or aricept) | 0 |
| ☐ | L6 | L5 and (@AD<20021213 or @PRAD<20021213 or @RLAD<20020213) | 17 |
| ☐ | L5 | L2 and (severe or MMSE or sMMSE or (mini-mental state)) | 18 |
| ☐ | L4 | L3 and (severe or MMSE or sMMSE or (mini-mental state)) | 0 |
| ☐ | L3 | L2 and acetylcholinesterase | 25 |
| ☐ | L2 | L1 and (alzheimer's) | 105 |
| ☐ | L1 | 514/37.icls. or 514/37.ccls. or 546/206.icls. or 546/206.ccls. | 888 |

END OF SEARCH HISTORY

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     FILE 'REGISTRY' ENTERED AT 09:18:26 ON 01 FEB 2008
L5             5 S DONEPEZIL
L6             1 S DONEPEZIL/CN

     FILE 'STNGUIDE' ENTERED AT 09:19:07 ON 01 FEB 2008

     FILE 'HCAPLUS' ENTERED AT 09:20:11 ON 01 FEB 2008
L7           893 S L6
L8         48870 S ALZHEIMER
L9        175115 S (MMSE OR (MINI-MENTAL STATE EXAMINATION) OR SEVERE)
L10          108 S L7 AND L8 AND L9

     FILE 'STNGUIDE' ENTERED AT 09:20:16 ON 01 FEB 2008

     FILE 'HCAPLUS' ENTERED AT 09:20:33 ON 01 FEB 2008
L11           36 S L10 AND (PY<2003 OR AY<2003 OR PRY<2003)
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```
=> s donepezil
L5            5 DONEPEZIL

=> s donepezil/cn
L6            1 DONEPEZIL/CN

=> file stnguide
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    10.76     139.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -24.00

FILE 'STNGUIDE' ENTERED AT 09:19:07 ON 01 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> file hcaplus
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FULL ESTIMATED COST                                     0.12     140.00

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CA SUBSCRIBER PRICE                                     0.00     -24.00

FILE 'HCAPLUS' ENTERED AT 09:20:11 ON 01 FEB 2008
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 1 Feb 2008  VOL 148 ISS 6
FILE LAST UPDATED: 31 Jan 2008  (20080131/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l6

L7          893 L6

=> s Alzheimer

L8        48870 ALZHEIMER

=> s (MMSE or (mini-mental state examination) or severe)
```

```
          533 MMSE
        16894 MINI
        67401 MENTAL
      1472697 STATE
        31903 EXAMINATION
            8 MINI-MENTAL STATE EXAMINATION
              (MINI(W)MENTAL(W)STATE(W)EXAMINATION)
       174630 SEVERE
L9     175115 (MMSE OR (MINI-MENTAL STATE EXAMINATION) OR SEVERE)

=> s l7 and l8 and l9

L10       108 L7 AND L8 AND L9

=> s s l10 and (PY<2003 or AY<2003 or PRY<2003)

MISSING OPERATOR S L10
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> file stnguide

COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                0.00     -24.00

FILE 'STNGUIDE' ENTERED AT 09:20:16 ON 01 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                                0.06     142.75

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CA SUBSCRIBER PRICE                                0.00     -24.00

FILE 'HCAPLUS' ENTERED AT 09:20:33 ON 01 FEB 2008
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 1 Feb 2008 VOL 148 ISS 6

FILE LAST UPDATED: 31 Jan 2008 (20080131/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l10 and (PY<2003 or AY<2003 or PRY<2003)

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      22927790 PY<2003
       4475620 AY<2003
       3950746 PRY<2003
L11          36 L10 AND (PY<2003 OR AY<2003 OR PRY<2003)
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=> file stnguide

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| CA SUBSCRIBER PRICE | 0.00 | -24.00 |

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FILE CONTAINS CURRENT INFORMATION.
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=> file stnguide

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| FULL ESTIMATED COST | 0.06 | 145.50 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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| CA SUBSCRIBER PRICE | 0.00 | -24.00 |

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=> file stnguide

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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> file stnguide

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| FULL ESTIMATED COST | 0.06 | 145.62 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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=> file stnguide

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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| FULL ESTIMATED COST | 0.06 | 145.68 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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| CA SUBSCRIBER PRICE | 0.00 | -24.00 |

FILE 'STNGUIDE' ENTERED AT 09:20:39 ON 01 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
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=> file stnguide

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.06 | 145.74 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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| CA SUBSCRIBER PRICE | 0.00 | -24.00 |

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> d l11 1-36 ti
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation and combination therapy of cyclohexanamines and acetylcholinesterase inhibitors for treatment of dementia

L11 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Methods and compositions using cholinesterase inhibitors for the treatment

of nervous system disorders and other conditions

L11 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil treatment of vascular dementia

L11 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Functional, cognitive and behavioral effects of donepezil in patients with moderate Alzheimer's disease

L11 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil for the treatment of behavioral symptoms in patients with Alzheimer's disease

L11 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Treatment with donepezil in Alzheimer patients with and without cerebrovascular disease

L11 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The preservation of function in Alzheimer's disease: Results from a 1-year, placebo-controlled study with donepezil

L11 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The efficacy and safety of donepezil in patients with moderate to severe Alzheimer's disease

L11 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Effects of long-term Donepezil therapy on rCBF of Alzheimer's patients

L11 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Quantitative EEG Changes in Alzheimer Patients during Long-Term Donepezil Therapy

L11 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Brain perfusion follow-up in Alzheimer's patients during treatment with acetylcholinesterase inhibitors

L11 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil versus vitamin E in Alzheimer's disease, Part 2: mild versus moderate-severe Alzheimer's disease

L11 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil and rivastigmine in the treatment of Alzheimer's disease: a best-evidence synthesis of the published data on their efficacy and cost-effectiveness

L11 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Management of Alzheimer's disease: defining the role of donepezil

L11 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Cognitive relapse after discontinuation of drug therapy in Alzheimer's disease: Cholinesterase inhibitors versus nootropics

L11 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The beneficial effect of cholinesterase inhibitors on patients suffering from Parkinson's disease and dementia

L11 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI [Effect of] Atrophy of the substantia innominata on magnetic resonance imaging and response to donepezil treatment in Alzheimer's disease

L11 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Cholinergic adverse effects of cholinesterase inhibitors in Alzheimer's disease: epidemiology and management

L11 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil in the treatment of Alzheimer's disease Long-term efficacy and safety

L11 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI EEG changes during long-term treatment with donepezil in Alzheimer 's disease patients

L11 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Ventricular measurements in computed tomography of responders and non-responders to donepezil in the treatment of Alzheimer's disease

L11 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Pharmacological treatment of non-cognitive disturbances in dementia disorders

L11 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Maintaining cognitive function in Alzheimer disease: how effective are current treatments?

L11 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease

L11 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Cognitive deficits in Alzheimer's disease: treatment with acetylcholinesterase inhibitor agents

L11 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Chronic donepezil treatment is associated with slowed cognitive decline in Alzheimer's disease

L11 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Efficacy of acetylcholinesterase inhibitors versus nootropics in Alzheimer's disease: A retrospective, longitudinal study

L11 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil, rivastigmine, and vitamin E in Alzheimer disease: a combined P300 event-related potentials/neuropsychologic evaluation over 6 months

L11 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil dose-dependently inhibits acetylcholinesterase activity in various areas and in the presynaptic cholinergic and the postsynaptic cholinoceptive enzyme-positive structures in the human and rat brain

L11 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Effects of donepezil on emotional/behavioral symptoms in Alzheimer 's disease patients

L11 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicenter open-label study

L11 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A comparative study in rats of the in vitro and in vivo pharmacology of the acetylcholinesterase inhibitors tacrine, donepezil and NXX-066

L11 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Perspectives in the management of Alzheimer's disease: clinical profile of donepezil

L11 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study

L11 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease

L11 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil (E2020): a new acetylcholinesterase inhibitor. Review of its pharmacology, pharmacokinetics, and utility in the treatment of Alzheimer's disease

=> d l11 1-36 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation and combination therapy of cyclohexanamines and acetylcholinesterase inhibitors for treatment of dementia
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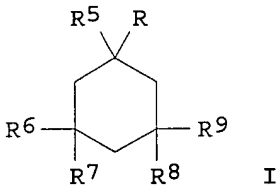

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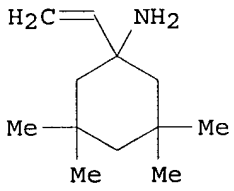

II

AB The invention relates to a drug combination therapy useful in the treatment of dementia associated with disorders of the central nervous system, e.g. to delay the onset or progression of Alzheimer's disease, cerebrovascular disease, or Down's syndrome, comprising a combination of a 1-aminocyclohexane derivative I [wherein R = An(CR1R2)mNR3R4; n + m = 0-2; A = alkylene, alkenylene, or alkynylene; R1 and R2 = independently H, alkyl, alkenyl, alkynyl, or (un)substituted aryl(alkyl); R3 and R4 = independently H, alkyl, alkenyl, alkynyl, etc.; or NR3R4 = azacycloalkyl or azacycloalkenyl; R5 = independently H, alkyl, alkenyl, or alkynyl; or R5 may combine with the C to which it is attached and an adjacent ring carbon to form a double bond; R6-R9 = independently H, (cyclo)alkyl, alkenyl, alkynyl, or (un)substituted aryl(alkyl); or R6-R9 may combine to form an alkylene or alkenylene bridge; and optical isomers, diastereomers, polymorphs, enantiomers, hydrates, pharmaceutically acceptable salts thereof], such as memantine or neramexane, and an acetylcholinesterase inhibitor (AChEI), such as galantamine, tacrine, donepezil, or rivastigmine. Examples include synthesis of cyclohexanamines and azabicycles and clin. trials of combination therapy of a cyclohexanamine with an AChEI. For instance, coupling of tri-Et phosphonoacetate and 3,3,5,5-tetramethylcyclohexanone in the presence of NaH in THF gave Et 2-(3,3,5,5-tetramethylcyclohexylidene)acetate (86%), which was reduced to the alc. (89%) using LiAlH4 in dry ether. Reductive addition of trichloroacetonitrile to the enol using NaH in di-Et ether (66%), followed by N-deprotection with NaOH in DMSO provided II•HCl (53%).

Combination therapy comprising memantine and donepezil was evaluated in a double blind study of 403 Alzheimer's disease patients. Patients treated with memantine and donepezil showed clin. and statistically significant improvement ($p<0.001$) in cognitive function ( Severe Impairment Battery Test) as compared to patients treated with donepezil and placebo, and showed significantly less decline ($p=0.028$) in daily function (AD Cooperative Study - Activities of Daily Living Inventory). The combination was safe and well tolerated, resulting in a similar incidence of treatment-emergent adverse events as donepezil/placebo.

AN 2004:368913 HCAPLUS <<LOGINID::20080201>>
DN 140:395498
TI Preparation and combination therapy of cyclohexanamines and acetylcholinesterase inhibitors for treatment of dementia
IN Moebius, Hans-Joerg
PA Merz Pharma G.m.b.H. & Co. K.-G.a.A., Germany; Marsden, John Christopher
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004037234 | A2 | 20040506 | WO 2003-GB4549 | 20031023 <-- |
| | WO 2004037234 | A3 | 20040805 | | |
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| | AU 2003274353 | A1 | 20040513 | AU 2003-274353 | 20031023 <-- |
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| | EP 1556019 | A2 | 20050727 | EP 2003-758338 | 20031023 <-- |
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| | CN 1720035 | A | 20060111 | CN 2003-80104613 | 20031023 <-- |
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| | ZA 2005003204 | A | 20060726 | ZA 2005-3204 | 20050420 <-- |
| | KR 777904 | B1 | 20071128 | KR 2005-707052 | 20050422 <-- |
| | NO 2005002462 | A | 20050720 | NO 2005-2462 | 20050523 <-- |
| | KR 2007087161 | A | 20070827 | KR 2007-716542 | 20070719 <-- |
| PRAI | US 2002-420918P | P | 20021024 <-- | | |
| | WO 2003-GB4549 | W | 20031023 | | |
| | KR 2005-707052 | A3 | 20050422 | | |

OS MARPAT 140:395498

L11 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Methods and compositions using cholinesterase inhibitors for the treatment of nervous system disorders and other conditions
AB The invention provides methods for treating and/or preventing Alzheimer's disease, psychiatric illnesses, encephalitis, meningitis, fetal alc. syndrome, Korsakoff's syndrome, anoxic brain injury, cardiopulmonary resuscitation injuries, diabetes, Sjogren's syndrome, mental retardation, developmental delay, menopause, strokes, macular degeneration, neuronal loss associated with macular degeneration, sleep disorders, severe Alzheimer's disease, jet lag, post-traumatic stress disorder, anxiety disorders, panic attacks,

obsessive-compulsive disorder, amnesia, and other disorders by administering to a patient in need thereof at least one cholinesterase inhibitor. The invention also provides novel pharmaceutical compns. that can be administered to the eyes or to the nose of patients. In one embodiment, the cholinesterase inhibitor is donepezil, a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof. In other embodiments, the cholinesterase inhibitor can be one or more of phenserine, tolserine, phenethylnorcymserine, ganstigmine, epastigmine, tacrine, physostigmine, pyridostigmine, neostigmine, rivastigmine, galantamine, citicoline, velnacrine, huperzine, metrifonate, heptastigmine, edrophonium, TAK-147, T-82, and upreazine.

AN 2004:354723 HCAPLUS <<LOGINID::20080201>>
DN 140:368732
TI Methods and compositions using cholinesterase inhibitors for the treatment of nervous system disorders and other conditions
IN Ieni, John; Pratt, Raymond
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004034963 | A2 | 20040429 | WO 2003-US15279 | 20030516 <-- |
| | WO 2004034963 | A3 | 20040722 | | |
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| | AU 2003298514 | A1 | 20040504 | AU 2003-298514 | 20030516 <-- |
| | US 2006018839 | A1 | 20060126 | US 2004-988600 | 20041116 <-- |
| | US 2007053976 | A1 | 20070308 | US 2006-523803 | 20060920 <-- |
| PRAI | US 2002-380852P | P | 20020517 <-- | | |
| | US 2003-447724P | P | 20030219 | | |
| | WO 2003-US15279 | W | 20030516 | | |
| | US 2004-988600 | A2 | 20041116 | | |
| | JP 2005-276222 | A | 20050922 | | |

OS MARPAT 140:368732

L11 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil treatment of vascular dementia
AB Cholinergic deficits are clinicopathol. hallmarks of Alzheimer's disease (DAT) and during the past decade have been the sole target for clin. effective treatments. By contrast, vascular dementia subtypes (VaD) are heterogeneous clin. syndromes, and therapeutic approaches have been directed toward control of vascular risk factors. Little attention has been paid to cholinergic deficits as a mechanism contributing to cognitive impairments in VaD as a potential target for treatment. The purpose of the study was to determine whether there are therapeutic benefits from long-term treatment with cholinesterase inhibitors among VaD patients. Ten VaD patients were diagnosed according to DSM-III-R and NINDS-AIREN criteria and classified into subtypes by neuroimaging. All were treated with titrated doses of donepezil for a mean interval of 15 mo. At baseline and follow-up clinic visits, patients underwent medical and neurol. examns., as well as neuropsycbol. testing including Mini-Mental Status Examns. (MMSE) and Cognitive Capacity Screening Examns. (CCSE). Cognitive statuses of 10 treated patients were then compared

before and after treatment. Net changes were expressed as annual MMSE score changes (.DELTA.MMSE/yr) and annual CCSE score changes (ΔCCSE/yr). Of the 10 treated VaD patients, cognitive improvements were found when comparisons were made before and after treatment. Ten treated patients also showed greater cognitive improvements, while untreated patients showed continued cognitive decline. This study suggests that cholinergic deficits in VaD are due to neuronal ischemic damage with loss of acetylcholine and that treatment of VaD with cholinesterase inhibitors is a rational therapy.

AN 2002:968232 HCAPLUS <<LOGINID::20080201>>
DN 138:33244
TI Donepezil treatment of vascular dementia
AU Meyer, John Stirling; Chowdhury, Munir H.; Xu, Gelin; Li, Yan-Sheng; Quach, Minh
CS Department of Neurology, Baylor College of Medicine, and Cerebrovascular Research Laboratories, Veterans Administration Medical Center, Houston, TX, USA
SO Annals of the New York Academy of Sciences (2002), 977(Alzheimer's Disease: Vascular Etiology and Pathology), 482-486 CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Functional, cognitive and behavioral effects of donepezil in patients with moderate Alzheimer's disease
AB The aim of this study was to investigate the efficacy and safety of donepezil in a subgroup of patients with Alzheimer's disease (AD) of moderate severity from a previous trial. Two hundred and seven patients with moderate AD (standardized Mini-Mental State Examination [sMMSE] score 10-17) were randomized to treatment in this 24-wk, double-blind, placebo-controlled trial. Patients received either donepezil, 5 mg/day for the first 28 days and 10 mg/day thereafter according to the clinician's judgement (n = 102), or placebo (n = 105). The primary outcome measure was the Clinician's Interview-Based Impression of Change with caregiver input (CIBIC-plus) at week 24 using a last observation carried forward (LOCF) anal. Baseline patient demographics were similar between treatment groups. Mean age was 74.3 yr (range 48-92). Least-squares (LS) mean sMMSE scores at baseline were 13.6±0.3 for the donepezil group and 13.9±0.3 for the placebo group. LS mean CIBIC-plus scores for donepezil-treated patients were improved from, or close to, baseline severity at all visits, and were significantly different from placebo at weeks 8, 12, 18, and 24 (week 24 LOCF mean difference = 0.53, p = 0.0003). LS mean change from baseline scores on the sMMSE and Severe Impairment Battery (SIB) for the donepezil group improved throughout the study, and were significantly different from placebo at each visit for the sMMSE (week 24 LOCF mean difference = 2.06, p = 0.0002) and from week 8 for the SIB (week 24 LOCF mean difference = -4.44, p = 0.0026). LS mean change scores on the Disability Assessment for Dementia remained at or above baseline levels throughout the study for the donepezil group, while the placebo group showed a steady decline; treatment differences were significant at each visit (week 24 LOCF mean difference = -9.25, p < 0.0001). LS mean change scores on the Neuropsychiatric Inventory 12-item total improved throughout the study for the donepezil group and were significantly different from placebo at weeks 4 and 24 (week 24 LOCF mean difference = 5.92, p = 0.0022). Eighty-one per cent of donepezil-treated and 89% of placebo-treated patients completed the trial, with 9% and 5%, resp., discontinuing due to adverse events (AEs). Eighty-two per cent of donepezil-treated and 80% of placebo-treated patients experienced AEs, the majority of which were rated mild in severity and, in general, were similar between treatment groups.

The significant treatment responses observed with donepezil in these patients reinforce the findings from earlier studies that show donepezil to have important benefits, compared with placebo, across functional, cognitive, and behavioral symptoms, with good tolerability, in patients with AD of moderate severity.

AN 2002:941314 HCAPLUS <<LOGINID::20080201>>
DN 138:19395
TI Functional, cognitive and behavioral effects of donepezil in patients with moderate Alzheimer's disease
AU Gauthier, S.; Feldman, H.; Hecker, J.; Vellas, B.; Emir, B.; Subbiah, P.
CS The Donepezil MSAD Study Investigators' Group, Alzheimer Disease Research Unit, McGill Centre for Studies in Aging, Verdun, QC, Can.
SO Current Medical Research and Opinion (2002), 18(6), 347-354
CODEN: CMROCX; ISSN: 0300-7995
PB LibraPharm Ltd.
DT Journal
LA English
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil for the treatment of behavioral symptoms in patients with Alzheimer's disease
AB Behavioral and psychol. symptoms of dementia (BPSD) are common manifestations in mid- and late-stage Alzheimer's disease (AD). Traditional treatments for BPSD are neuroleptics and sedatives, which are not devoid of serious adverse effects. A number of studies show beneficial effects in the treatment of BPSD with acetylcholinesterase inhibitors (AChEI). The present study aimed to evaluate the effect of donepezil (using the generic drug Memorit) as monotherapy for AD patients suffering from BPSD. Twenty-eight consecutive patients followed at the Memory Outpatient Clinic and Psychogeriatric Department of the Abarbanel Mental Health Center were treated with donepezil for 6 mo. Starting dose was 5 mg daily during the first 4 wk and continuation with 10 mg daily thereafter. Treatment effects were evaluated using the Mini Mental State Examination (MMSE), the Neuro-Psychiatric Inventory (NPI), and the Clin. Global Impression of Change Scale (CGIC) caregiver version. Twenty-four of 28 patients completed the study. Of these, five patients needed addnl. rescue neuroleptic treatment due to incomplete response. The mean dose of donepezil was 9.10 mg/day (median 10 mg/day). The overall NPI improved significantly from 33.4 to 21.2 ($p = 0.008$). The mean CGIC at study's end was 3.0 (mild improvement). The cognitive scores did not change significantly. When compared to the patients who completed the study, patients who discontinued had higher mean scores on the irritability and agitation subscales of the NPI, they were older, and they had longer disease duration and lower MMSE mean scores. Three adverse events were recorded: one syncope causing a toe phalanx fracture and gastrointestinal complaints that resolved over time in two addnl. patients. Acetylcholinesterase inhibitors should be considered for the treatment of BPSD before neuroleptic treatment is instituted in AD patients with low levels of irritability and agitation.
AN 2002:933238 HCAPLUS <<LOGINID::20080201>>
DN 139:159763
TI Donepezil for the treatment of behavioral symptoms in patients with Alzheimer's disease
AU Paleacu, Diana; Mazeh, Doron; Mirecki, Ilona; Even, Michael; Barak, Yoram
CS Neurological Service and Memory Clinic, Abarbanel Mental Health Center, Bat-yam, Israel
SO Clinical Neuropharmacology (2002), 25(6), 313-317
CODEN: CLNEDB; ISSN: 0362-5664
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Treatment with donepezil in Alzheimer patients with and without cerebrovascular disease
AB Donepezil, a selective acetylcholinesterase inhibitor, is approved for the symptomatic treatment of mild to moderate Alzheimer's disease (AD). In a post-marketing surveillance (PMS) study in Germany, patients under routine treatment conditions were observed while treatment was switched from other antidementia drugs (i.e., nootropics) to donepezil. A total of 913 patients were enrolled (60.1% female, mean age 73.4 yr, mean Mini-Mental Status Examination [MMSE] 18.0), and were treated with donepezil (5 or 10 mg/day according to recommended dosing). Seven-hundred nine of 913 (77.1%) patients had been pretreated with other antidementive drugs (piracetam, memantine, ginkgo, and others). In 29.6% of patients, investigators documented concomitant cerebrovascular disease (CVD+) according to their clin. judgment. Observation period was 3 mo for the individual patient. Efficacy parameters were changes in MMSE, global clin. (investigators) judgment of efficacy, and a clin. judgment about the patients' quality of life (QoL). Adverse events were also analyzed. The objective of the present investigation was to compare-in a "real-life" setting-the differential efficacy and tolerability of donepezil in AD patients with and without concomitant cerebrovascular disease. After 3 mo, patients had improved by a mean MMSE change from baseline of 2.2 points (CVD+: 2.4 pts, CVD-: 2.1 pts). QoL was judged "improved" in 70.0% of patients (CVD+: 72.5%, CVD-: 69.6%). Adverse events were reported in 85/913 (9.3%) of patients (CVD+: 11.2%, CVD-: 7.9%). Reported adverse events were substantially less than reported previously in controlled clin. trials. This suggests that donepezil therapy is effective and well tolerated in AD patients, both with and without concomitant cerebrovascular disease.
AN 2002:839425 HCAPLUS <<LOGINID::20080201>>
DN 139:95222
TI Treatment with donepezil in Alzheimer patients with and without cerebrovascular disease
AU Frolich, L.; Klinger, T.; Berger, F. M.
CS Klinik fur Psychiatrie und Psychotherapie I, Klinikum der Universitat Frankfurt am Main, Frankfurt am Main, D-60528, Germany
SO Journal of the Neurological Sciences (2002), 203-204, 137-139
CODEN: JNSCAG; ISSN: 0022-510X
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The preservation of function in Alzheimer's disease: Results from a 1-year, placebo-controlled study with donepezil
AB The progressive loss of functional ability that is a common feature of Alzheimer's disease (AD) leads to an increased need for patient care. This 1-yr, double-blind, placebo-controlled study examined the effects of donepezil (10 mg/d) on preserving function in 431 patients with mild to moderate AD. Outcome measures were the AD Functional Assessment and Change Scale, the MMSE, and CDR. Donepezil extended the time to clin. evident functional decline by 5 mo over placebo. At 48 wk, the probability of donepezil patients remaining in the study with no clin. evident functional loss was 51% compared with 35% for placebo patients. While patients continued to show disease progression over time, donepezil was associated with a 38% reduction in the risk of functional decline compared with placebo. This study showed that preservation of function is a measurable outcome of donepezil treatment, reflective of cognitive status, and easily assessed in the clinic setting.
AN 2002:722590 HCAPLUS <<LOGINID::20080201>>

DN 137:273099
TI The preservation of function in Alzheimer's disease: Results from a 1-year, placebo-controlled study with donepezil
AU Mohs, R. C.; Doody, R. S.; Morris, J. C.; Ieni, J. R.; Rogers, S. L.; Perdomo, C. A.; Pratt, R. D.
CS Mount Sinai School of Medicine, Bronx VA Medical Center, New York, USA
SO Research and Practice in Alzheimer's Disease (2002), 6, 308-315 CODEN: RPADBW; ISSN: 1284-8360
PB Serdi Edition
DT Journal
LA English
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The efficacy and safety of donepezil in patients with moderate to severe Alzheimer's disease
AB A review. The evaluation of effective and safe treatments for patients in the later stages of Alzheimer's disease has received little study. We conducted a 24-wk, double-blind, placebo-controlled study to examine the efficacy and safety of donepezil (n=144) compared with placebo (n=146) in patients with moderate to severe AD (sMMSE score 5-17). The primary outcome measure was the Clinician's Interview-Based Impression of Change with care giver input (CIBIC+) and secondary outcome measures included assessments of cognition, function, and behavior. Donepezil significantly improved CIBIC+ scores compared with placebo at all visits and at week 24 LOCF. Secondary outcome measures were all significant at week 24 LOCF. Eight-four percent of donepezil- and 86% of placebo-treated patients completed the trial, with 8% of donepezil- and 6% of placebo-treated patients discontinuing due to an adverse event. This study showed that donepezil is a safe and efficacious treatment for patients with moderate to severe AD.
AN 2002:722589 HCAPLUS <<LOGINID::20080201>>
DN 137:272691
TI The efficacy and safety of donepezil in patients with moderate to severe Alzheimer's disease
AU Feldman, H.; Gauthier, S.; Hecker, J.; Vellas, B.; Subbiah, P.; Whalen, E.; Emir, B.
CS Division of Neurology, Clinic for Alzheimer's Disease and Related Disorders, UBC Hospital, Vancouver, BC, V6T2B5, Can.
SO Research and Practice in Alzheimer's Disease (2002), 6, 302-307 CODEN: RPADBW; ISSN: 1284-8360
PB Serdi Edition
DT Journal; General Review
LA English
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Effects of long-term Donepezil therapy on rCBF of Alzheimer's patients
AB The recent introduction of acetylcholinesterase inhibitors (AChEIs) therapy for Alzheimer's Disease (AD) has led to the need to assess the brain's response to the therapy on an objective, neurophysiol. basis. Brain perfusion single photon emission computed tomog. (SPECT) was used in an open-label study to evaluate the effect of chronic Donepezil administration to a group of patients affected by mild to moderate AD, compared to a group of AD patients not receiving AChEIs and kept under observation for a similar period. Twenty-five consecutive patients with probable AD (National Institute of Neurol. and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association criteria) (19 women, 6 men; mean age: 74.2 ± 7.2; mean Mini-Mental State Examination score, MMSE: 19.8 ± 3.5) underwent (t0) brain SPECT with 99mTc-hexamethylpropylene-amine-oxime by a brain-dedicated,

high-resolution camera and were re-evaluated (t1) after 11 ± 2.6 mo of chronic Donepezil administration (5 mg/day) (treated group). Thirteen AD patients (9 women, 4 men, mean age: 71.4 ± 5.7, MMSE score: 20.6 ± 3.5) were not treated with AChEIs and served as controls (untreated group). They were subjected to the same evaluation after 13 ± 1.4 mo as the treated group. Statistical parametric mapping (SPM) was employed to analyze SPECT findings. The MMSE score declined significantly ($P < 0.01$) from t0 to t1 both in untreated (from 20.6 ± 3.5 to 17.8 ± 4.4) and in treated (from 19.8 ± 3.5 to 17.8 ± 4.1) group. At t0, the untreated group showed higher regional cerebral blood flow (rCBF) than the treated group in a frontal and a frontal-parietal region of the left hemisphere. Between t0 and t1, significant rCBF reduction was observed in the temporal lobe and occipital-temporal cortex of the left hemisphere in the untreated group, whereas no significant change was observed in the treated group. The rCBF of the two groups did not significantly differ at t1. By covariate SPM anal. between t0 and t1 in treated patients, MMSE score changes correlated significantly with rCBF changes in a large left frontal-temporal region. Brain perfusion is preserved in AD patients undergoing chronic Donepezil therapy while it is reduced in untreated patients. SPECT is a promising tool with which to assess the impact of AChEI therapy on brain functioning of AD patients.

AN 2002:705859 HCAPLUS <<LOGINID::20080201>>
DN 137:242076
TI Effects of long-term Donepezil therapy on rCBF of Alzheimer's patients
AU Nobili, Flavio; Vitali, Paolo; Canfora, Michela; Girtler, Nicola; De Leo, Caterina; Mariani, Giuliano; Pupi, Alberto; Rodriguez, Guido
CS Clinical Neurophysiology Service, Department of Internal Medicine, University of Genoa, Genoa, I-16132, Italy
SO Clinical Neurophysiology (2002), 113(8), 1241-1248
CODEN: CNEUFU; ISSN: 1388-2457
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Quantitative EEG Changes in Alzheimer Patients during Long-Term Donepezil Therapy
AB Twenty patients affected with probable mild-to-moderate Alzheimer 's disease (AD; NINCDS-ADRDA criteria; 14 women and 6 men, mean age 75.2±7.1 yr) who regularly received an oral acetylcholinesterase inhibitor (AChEI; donepezil 5 mg/day; Dz group) were compared with a control group of 11 AD patients (6 women and 5 men, mean age 73.5±6.0 yr) diagnosed and followed up in the pre-AChEIs era (C group). At basal evaluation (t0), the 2 groups were comparable for age, education, and severity of disease (Global Deterioration Scale). All patients underwent quant. EEG (qEEG, average reference, 10-20 International System), and were reexamd.
about 1 yr later (t1; i.e., after 12.3±3.6 mo the Dz group, and after 13.7±3.9 mo the C group). Log-transformed values of two qEEG bands, i.e., 2-6 and 6.5-12 Hz, were averaged between adjacent channels (frontal F3 and F7, F4 and F8; parietotemporal P3 and T7, P4 and T8) to obtain a qEEG ratio (6.5-12/2-6 Hz.) from one frontal and one temporoparietal region in each hemisphere. Neuropsychol. impairment was summarized by the Mini-Mental Status Examination (MMSE). At t0, both the MMSE score and the qEEG ratio values were somewhat higher in the C than in the Dz group, although nonsignificantly. Between t0 and t1, the MMSE score decreased significantly ($p < 0.01$) more in the C group (-4.36±2.25) than in the Dz group (-1.45±2.16), as did the qEEG ratio in the right frontal region ($p < 0.01$), whereas in the left frontal region the significance level was not reached ($p = 0.02$). Between t0 and t1, the qEEG ratio difference in both frontal regions and in the right

temporoparietal region significantly correlated with the MMSE difference ($p < 0.01$), but neither with time between examns. nor with the difference on the Visual Search Test score. Long-term treatment with Dz led to a lesser deterioration of qEEG, paralleling a milder neuropsychol. decline. The effect was significant in frontal regions, possibly because they are relatively spared during the mild-to-moderate phases of the disease.

AN 2002:663881 HCAPLUS <<LOGINID::20080201>>
DN 138:362491
TI Quantitative EEG Changes in Alzheimer Patients during Long-Term Donepezil Therapy
AU Rodriguez, Guido; Vitali, Paolo; De Leo, Caterina; De Carli, Fabrizio; Girtler, Nicola; Nobili, Flavio
CS Department of Internal Medicine, Clinical Neurophysiology, University of Genoa, Genoa, Italy
SO Neuropsychobiology (2002), 46(1), 49-56
CODEN: NPBYAL; ISSN: 0302-282X
PB S. Karger AG
DT Journal
LA English
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Brain perfusion follow-up in Alzheimer's patients during treatment with acetylcholinesterase inhibitors
AB Transient cognitive and behavioral stabilization of patients with Alzheimer's disease (AD) is the main goal of long-term acetyl-cholinesterase inhibitor (AChEI) therapy, but response to treatment is variable and, indeed, only some of the patients are stabilized. This is usually assessed by means of clin. and neuropsychol. scales, whereas functional neuroimaging could allow objective evaluation of the topog. correlates of the effect of therapy on brain functioning. The aim of this study was to evaluate brain perfusion changes by SPECT in AD patients during chronic AChEI therapy in relation to their cognitive evolution. Forty-seven consecutive outpatients with mild-to-moderate probable AD (as defined by the National Institute of Neurol. and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association and the Diagnostic and Statistical Manual of Mental Disorders [4th edition criteria] and a score of ≥15 on the Mini-Mental State Examination [ MMSE]) were enrolled in 2 centers over a 1-y period and underwent SPELT with 99mTc-hexamethylpropylene-amine oxime at the time of enrollment (t0). All of them started AChEI therapy. Nine patients were lost at follow-up, and drugs were withdrawn from 3 patients. Of the remaining 35 patients, who received regular AChEI therapy (donepezil, 5 or 10 mg/d; rivastigmine, 6 or 9 mg/d) throughout the observation period, only the 31 patients receiving donepezil were considered to avoid the possible confounding effect of different drugs. The 31 patients completed the study and a second SPELT examination was performed 15.0±3.0 mo later (t1). They were divided into stabilized (17 patients) and nonstabilized (14 patients) subgroups on the basis of the min. expected annual rate of decline of the MMSE score, derived from a meta-anal. of the literature. SPELT data were analyzed by means of statistical parametric mapping. At baseline, the stabilized and nonstabilized patients were comparable for age, sex distribution, education, MMSE scores, memory impairment (selective reminding test [SRT]), apolipoprotein E genotype, AChEI dose regimen, and SPELT findings. The SRT scores decreased significantly ($P < 0.01$) in the nonstabilized subgroup but not in the stabilized subgroup. No significant difference was found between the baseline and repeated SPELT data in the stabilized subgroup. In contrast, in the nonstabilized subgroup a significant perfusion reduction was found in the frontal, temporal, and parietal superficial cortex and in the occipital precuneus in the right hemisphere and in the frontal and mesial temporal cortex in the left hemisphere. On repeated SPELT, regional

cerebral blood flow was significantly lower in a left frontal region in the nonstabilized group than in the stabilized group. The regional cerebral blood flow decreases in several cortical regions in AD patients with cognitive deterioration despite longterm AChEI therapy, similar to that observed in untreated patients, whereas it remains stable in AD patients with stabilized cognitive performance during therapy.

AN 2002:660289 HCAPLUS <<LOGINID::20080201>>
DN 137:210850
TI Brain perfusion follow-up in Alzheimer's patients during treatment with acetylcholinesterase inhibitors
AU Nobili, Flavio; Koulibaly, Malick; Vitali, Paolo; Migneco, Octave; Mariani, Giuliano; Ebmeier, Klaus; Pupi, Alberto; Robert, Philippe H.; Rodriguez, Guido; Darcourt, Jacques
CS Clinical Neurophysiology, Department of Internal Medicine, University of Genoa, Genoa, Italy
SO Journal of Nuclear Medicine (2002), 43(8), 983-990
CODEN: JNMEAQ; ISSN: 0161-5505
PB Society of Nuclear Medicine
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil versus vitamin E in Alzheimer's disease, Part 2: mild versus moderate-severe Alzheimer's disease
AB Early studies showed that the latency of P300 (P3) event related potential increases or diminishes when anticholinergic drugs are administered. We tested the hypothesis that new cholinesterase inhibitors like Donepezil (DPZ) may have an effect on the often abnormal P300 of patients with Alzheimer's Disease (AD), and therefore, that P300 recordings might simplify the evaluation of responses to cholinesterase inhibitor in patients with mild and moderate-severe AD. We evaluated 60 patients with AD: 30 patients with "mild" (Mini Mental State Examination 26-19) and 30 patients with "moderate-severe" (Mini Mental State Examination 18-10), according to the National Institute of Neurol. and Communicative Disorders and Alzheimer's Disease and Related Disorders Association criteria in comparison with 40 age-matched controls. All subjects underwent P300 recordings and neuropsychol. examns. (Alzheimer's Disease Assessment Scale-Cognition and Wechsler Adult Intelligence Scale) during the 6-mo follow-up. Patients were divided into four groups of 15 patients each: Group I DPZ (10 mg/day) and Group I Vitamin E (2000 IU/day) with "mild" AD; Group II DPZ and Group II Vitamin E with "moderate-severe" AD and same drug dosages. In patients treated with Vitamin E, we observed P3 latency increments (delta) by 11.8 ± 1.8 ms in Group I and by 12.8 ± 2.8 ms in Group II at 6 mo; neuropsychol. test scores significantly worsened at 6 mo ($p < 0.001$) in Group II patients. Donepezil induced significant P3 latency redns. (1 1.2 ± 2.4 ms) in nine patients of Group I and all patients of Group II (16.1 ± 4.0 ms), reaching a maximum at 3 mo (23.2 ± 2.7 ms). Alzheimer's Disease Assessment Scale-Cognition and Wechsler Adult Intelligence Scale scores improved during the same period, and the difference between Vitamin E and DPZ treated patients was highly significant for P3 (anal. of variance) and for P3-Alzheimer's Diseases Assessment Scale-Cognition (anal. of covariance) with $p < 0.001$ for pooled groups of patients with AD and Group II (DPZ) vs. Group II (Vitamin E). Combined P3 event related potentials measurements, neuropsychol. test comparison evidences significant effects of DPZ in mild and in moderate-severe AD.

AN 2002:659776 HCAPLUS <<LOGINID::20080201>>
DN 137:210848
TI Donepezil versus vitamin E in Alzheimer's disease, Part 2: mild versus moderate-severe Alzheimer's disease
AU Onfrj, Marco; Thomas, Astrid; Luciano, Anna Lisa; Iacono, Diego; Di Rollo, Andrea; D'Andreamatteo, Giordano; Di Iorio, Angelo

CS Department of Oncology and Neuroscience, Institute of Neurophysiopathology, University of "G.D'Annunzio", Italy
SO Clinical Neuropharmacology (2002), 25(4), 207-215
CODEN: CLNEDB; ISSN: 0362-5664
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil and rivastigmine in the treatment of Alzheimer's disease: a best-evidence synthesis of the published data on their efficacy and cost-effectiveness
AB A review. Various drugs have been approved for the treatment of Alzheimer's disease (AD) in the United States and Canada, including donepezil and rivastigmine, although questions remain as to their efficacy, effectiveness, and long-term benefits. The goal of this study was to conduct a best-evidence synthesis of data on the efficacy and cost-effectiveness of donepezil and rivastigmine in the treatment of AD. Relevant published randomized controlled trials (RCTs) and Phase IV open-label extension studies (excluding abstrs.) were identified through searches of MEDLINE, HealthSTAR, and PsycINFO for the period Jan. 1984 to Oct. 2001. The bibliogs. of retrieved articles were searched for addnl. publications. For inclusion in the best-evidence synthesis, clin. trials had to pass a blinded quality assessment (score ≥5 on the Jadad scale) and use National Institute of Neurol. and Communicative Disease and Stroke-Alzheimer's Disease and Related Disorders Association diagnostic criteria. Economic studies were selected using National Health Service Center for Reviews and Dissemination criteria for reporting critical summaries of economic evaluations. Nine RCTs of donepezil and 2 of rivastigmine were identified and met inclusion criteria for the best-evidence synthesis. Eight donepezil trials and both rivastigmine trials included patients with mild AD (Mini-Mental State Examination [ MMSE] score, 15-27) or moderate AD (MMSE score, 8-14); 1 donepezil trial included patients with moderate or severe AD ( MMSE score, 0-7). In the RCTs of donepezil, the mean decrease in scores on the Alzheimer's Disease Assessment Scale-cognitive sub-scale (ADAS-cog) was greater with active treatment than with placebo (lower scores indicate less cognitive deterioration). In the RCTs of rivastigmine, ADAS-cog scores decreased over the follow-up period with both active treatment and placebo; however, scores decreased more with active treatment. Three Phase IV studies of donepezil and 1 Phase IV study of rivastigmine were identified. Their results were consistent with those of the RCTs. Ten economic studies (7 donepezil, 3 rivastigmine) were identified and reviewed. In 4 of the donepezil studies and all 3 rivastigmine studies, use of the drug cost less than a no-drug strategy. The efficacy data indicate that both donepezil and rivastigmine can delay cognitive impairment and deterioration in global health for at least 6 mo in patients with mild to moderate AD. Patients receiving active treatment will have more favorable ADAS-cog scores for at least 6 mo, after which their scores will begin to converge with those of patients receiving placebo. Differences in methodol., types of direct or indirect costs included, and sources of cost data made it difficult to compare and synthesize findings of the economic studies; therefore, the cost-effectiveness data are inconclusive.
AN 2002:591114 HCAPLUS <<LOGINID::20080201>>
DN 137:149694
TI Donepezil and rivastigmine in the treatment of Alzheimer's disease: a best-evidence synthesis of the published data on their efficacy and cost-effectiveness
AU Wolfson, Christina; Oremus, Mark; Shukla, Vijay; Momoli, Franco; Demers, Louise; Perrault, Anne; Moride, Yola
CS Centre for Clinical Epidemiology and Community Studies, S.M.B.D. Jewish

General Hospital, Can.
SO Clinical Therapeutics (2002), 24(6), 862-886
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal; General Review
LA English
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Management of Alzheimer's disease: defining the role of donepezil
AB A review. Alzheimer's disease affects 15 million people worldwide. As the elderly population grows, the incidence of Alzheimer's disease will also increase. It is estimated that by 2010, 40 million US citizens will be over the age of 65 yr and by 2040, it is predicted that 14 million US citizens will have Alzheimer's disease. There is currently no treatment which stops or delays the progression of this condition; however, anticholinesterase therapy provides some symptomatic relief. The cognitive impairment experienced by patients with Alzheimer's disease is partially due to degeneration of cholinergic pathways within the CNS and therefore symptomatic treatments have focused on restoring cholinergic inputs. Donepezil is a second generation anticholinesterase drug which reduces cortical acetylcholinesterase activity and improves, or at least slows the decline in, cognitive functioning in patients with Alzheimer's disease. In patients with mild to moderate Alzheimer's disease, treatment with donepezil (5 to 10 mg/day) for 1 yr extended the median time to a clin. evident functional decline by 5 mo compared with treatment with placebo. In addition, patients receiving donepezil have also shown significant improvement in ratings of global function, cognition, activities of daily living and disease severity over a 1-yr period ($p < 0.05$ in each case). In patients with moderate to severe Alzheimer's disease, donepezil significantly improved ratings of behavior compared with placebo ($p < 0.05$). Donepezil treatment is associated with the well recognized adverse events which accompany cholinergic therapy. The most frequently reported adverse events with donepezil treatment are gastrointestinal complaints such as nausea, diarrhea and vomiting, and CNS conditions including dizziness, headache and insomnia. These adverse events are typically mild and transient. Preliminary data from a direct comparison of donepezil and rivastigmine suggests that donepezil may exhibit an improved tolerability profile compared with rivastigmine. Recent data suggest that use of donepezil is associated with a significant delay in the time to institutionalization. Data from modeling and pharmacoeconomic studies also predict that use of donepezil may lead to a reduction in costs. However, it is likely that these savings will be distributed across multiple healthcare and non-healthcare systems and may not be fully represented in the budgets of those who are responsible for the direct costs of providing this medication. Donepezil is the only cholinesterase inhibitor currently available in a once daily formulation and with a relatively simple dose escalation schedule. This regimen coupled with a good tolerability profile makes donepezil a first-line treatment for patients with mild to moderate Alzheimer's disease. However, only direct comparisons between donepezil and other second generation anticholinesterases will provide definitive data which can be used to maximize patient outcomes. In addition, wider clin. experience with donepezil may help to identify a subgroup of patients who respond strongly to treatment thus improving patient care and reducing costs.
AN 2002:217914 HCAPLUS <<LOGINID::20080201>>
DN 136:334646
TI Management of Alzheimer's disease: defining the role of donepezil
AU Ibbotson, Tim; Goa, Karen L.

CS Adis International Limited, Auckland, N. Z.
SO Disease Management & Health Outcomes (2002), 10(1), 41-54
CODEN: DMHOFV; ISSN: 1173-8790
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Cognitive relapse after discontinuation of drug therapy in Alzheimer's disease: Cholinesterase inhibitors versus nootropics
AB In a cross-sectional study of outpatients diagnosed with dementia of the Alzheimer type who had been treated with a broad variety of drugs supposed to improve cognition or to delay cognitive decline, we have investigated the effects of abruptly discontinuing therapy on cognition. Termination of therapy with any cholinesterase inhibitor was associated with a cognitive decline during the following 6-7 wk which was significantly more pronounced than that experienced by patients who had received nootropic drugs or calcium channel blockers (3.41 vs. 1.17 points on the ADAS-Cog scale; -1.14 vs. -0.06 points on the MMSE scale). This effect was not modified by gender, apolipoprotein E genotype, or the extent of ventricular enlargement on CT scans. Its magnitude was comparable to the cognitive response observed in published clin. trials when cholinesterase therapy commenced, and also with the data obtained during a 6-wk placebo washout phase.
AN 2002:140960 HCAPLUS <<LOGINID::20080201>>
DN 136:288980
TI Cognitive relapse after discontinuation of drug therapy in Alzheimer's disease: Cholinesterase inhibitors versus nootropics
AU Rainer, M.; Mucke, H. A. M.; Kruger-Rainer, C.; Kraxberger, E.; Haushofer, M.; Jellinger, K. A.
CS Memory-Clinic and Department of Psychiatry, Donauspital, Sozialmedizinisches Zentrum Ost, Vienna, Austria
SO Journal of Neural Transmission (2001), 108(11), 1327-1333
CODEN: JNTRF3; ISSN: 1435-1463
PB Springer-Verlag Wien
DT Journal
LA English
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI The beneficial effect of cholinesterase inhibitors on patients suffering from Parkinson's disease and dementia
AB Patients suffering from Parkinson's disease (PD), often develop dementia (PDD). Their brain histol. reveals Alzheimer's disease (AD) like changes and decreased cholin-acetyl transferase (ChAT) activity, in addition to typical PD changes. This cholinergic deficiency has been related to the degree of mental decline. As centrally acting cholinesterase inhibitors (ChEIs) provide cognitive and non-cognitive improvement for AD patients, the same therapeutic effect was hypothesized for PDD patients as well. The goal of this study was to assess the effect of ChEIs on both the cognitive and motor state of PDD patients. An open study was conducted. Eleven consecutive PDD patients (M/F 6/5 mean age 75y) were found eligible for inclusion. They were treated for 26 wk with tacrine (7 patients) and donepezil (4 patients) as add-on to their regular anti PD drugs. Cognitive assessment was performed at baseline and endpoint by Mini-Mental-State-Examination (MMSE) and Alzheimer 's-Disease-Assessment-Scale (ADAS-cog). Global Deterioration Scale (GDS) was performed to evaluate active daily living (ADL). Motor evaluation was performed using Short Parkinson Evaluation Scale (SPES) at baseline and end-point. Statistical anal. used Student's paired t-test, ANOVA with repeated measures and Pearson correlation coefficient ChEIs treated PDD

patients showed improvement in their cognitive state. Mean ADAS-cog improved significantly by 3.2 points ($p < 0.012$). Mean MMSE and GDS improved non-significantly by 1.2 and 0.2 points resp. There was no change in motor function as evident by mean SPES scores, 16.5 at baseline and endpoint. Five individuals actually demonstrated motor improvement under ChEIs. We conclude that ChEIs have a beneficial effect on the cognitive state of PDD patients without aggravating motor function.

AN 2002:140959 HCAPLUS <<LOGINID::20080201>>
DN 136:288979
TI The beneficial effect of cholinesterase inhibitors on patients suffering from Parkinson's disease and dementia
AU Werber, E. A.; Rabey, J. M.
CS Department of Neurology, Assaf Harofeh Medical Center, Zerifin, Israel
SO Journal of Neural Transmission (2001), 108(11), 1319-1325
CODEN: JNTRF3; ISSN: 1435-1463
PB Springer-Verlag Wien
DT Journal
LA English
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI [Effect of] Atrophy of the substantia innominata on magnetic resonance imaging and response to donepezil treatment in Alzheimer's disease
AB The effect of atrophy of the substantia innominata on magnetic resonance imaging (MRI), reflecting degeneration of cholinergic neurons in the nucleus basalis of Meynert, may be an in vivo marker of cholinergic damage. This work investigated whether the MRI features of the substantia innominata predict responses to donepezil treatment in Alzheimer 's patients. The thickness of the substantia innominata was measured by coronal T2-weighted MRI through the anterior commissure. Patients treated with donepezil were divided into 2 groups (responders and nonresponders) based on changes in Mini-Mental State Examination (MMSE) scores. Atrophy of the substantia innominata was more pronounced in responders than nonresponders. There was an inverse correlation between thickness of the substantia innominata and MMSE changes. MRI anal. of the substantia innominata may be a simple and practical method for the selection of possible treatment responders.
AN 2002:86859 HCAPLUS <<LOGINID::20080201>>
DN 137:584
TI [Effect of] Atrophy of the substantia innominata on magnetic resonance imaging and response to donepezil treatment in Alzheimer's disease
AU Hanyu, Haruo; Tanaka, Yuriko; Sakurai, Hirofumi; Takasaki, Masaru; Abe, Kimihiko
CS Department of Geriatric Medicine, Tokyo Medical University, Tokyo, 160-0023, Japan
SO Neuroscience Letters (2002), 319(1), 33-36
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Cholinergic adverse effects of cholinesterase inhibitors in Alzheimer's disease: epidemiology and management
AB A review. Cholinergic adverse effects of acetylcholinesterase inhibitors (AChEIs) are caused by their central and peripheral pharmacol. actions on a variety of organ tissues. Gastrointestinal adverse effects predominate and these were relatively common in the phase II and III randomized clin. trials of AChEIs for the treatment of probable Alzheimer's

disease. However, in these studies forced and rapid titration of drugs was used, which is not the case in clin. practice. Although there is a risk of pharmacodynamic interactions with other drugs leading to enhanced cholinergic adverse effects, very few of these interactions have proven to be clin. significant. Unresolved issues include the mechanism of syncope and neuromuscular weakness, which should be resolved through structured pharmacovigilance programs and clin. studies. Loss of bodyweight may prove to be a long term significant complication. As a class, the AChEIs have proven to be well tolerated in the symptomatic treatment of Alzheimer's disease in its mild-to-moderately severe stages. The incidence and clin. significance of cholinergic adverse events will need to be carefully studied if the drugs are used for indications other than Alzheimer's disease.

AN 2002:74011 HCAPLUS <<LOGINID::20080201>>
DN 136:272525
TI Cholinergic adverse effects of cholinesterase inhibitors in Alzheimer's disease: epidemiology and management
AU Gauthier, Serge
CS Alzheimer's Disease Research Unit, McGill Centre for Studies in Aging, Montreal, QC, H4H 1R3, Can.
SO Drugs & Aging (2001), 18(11), 853-862
CODEN: DRAGE6; ISSN: 1170-229X
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil in the treatment of Alzheimer's disease Long-term efficacy and safety
AB The aim of this study was to evaluate the long-term efficacy, safety and tolerability of donepezil in the treatment of Alzheimer's disease (AD). Twenty-five patients (15 females and 10 males) with mild to moderate AD, according to DSM IV criteria, were recruited in the study. The principal efficacy measures were Alzheimer Disease Assessment Scale-cognitive subscale score (ADAS-cog), Mini Mental State Examination (MMSE) and Phys. Self-Maintenance Scale (PSMS). Patients were treated with donepezil 5 mg/day for 1 mo, after which an increase to 10 mg/day was encouraged. Evaluations were carried out prior to the start of the treatment and every 3 mo for a period of 1 yr. A significant improvement from baseline score of cognitive performances was seen through Week 24. Beginning with Week 36, performances declined relative to baseline, indicating continued disease progression. Donepezil improved cognition and global functioning and was well tolerated especially considered the long duration of the observation period.

AN 2002:59805 HCAPLUS <<LOGINID::20080201>>
DN 136:257156
TI Donepezil in the treatment of Alzheimer's disease Long-term efficacy and safety
AU Rocca, Paola; Cocuzza, Elena; Marchiaro, Livio; Bogetto, Filippo
CS Department of Neuroscience, Psychiatric Section, University of Turin, Turin, 10126, Italy
SO Progress in Neuro-Psychopharmacology & Biological Psychiatry (2001), Volume Date 2002, 26(2), 369-373
CODEN: PNPPD7; ISSN: 0278-5846
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI EEG changes during long-term treatment with donepezil in Alzheimer

's disease patients
AB In this pilot study, we examined the long-term treatment effect of donepezil on the quant. EEG (qEEG) in 12 Alzheimer's disease patients. The qEEGs of the mean absolute and relative amplitudes of beta 1, alpha, theta and delta activities were obtained at baseline and during donepezil treatment. Comparisons of awake qEEG prior to and during treatment were performed using a 2-way anal. of variance (ANOVA) with repeated measures. In patients with mild dementia (n = 5), the qEEG anal. showed a significant reduction of the mean absolute theta activity (p = 0.05) by donepezil, particularly in frontal and temporo-parietal areas. In patients with moderate/severe dementia (n = 7), a significant decrease in the mean absolute beta 1 activity (p = 0.02), particularly in the frontal and occipital areas may be attributed to disease progression which was not counteracted by the long-term treatment. The differences in qEEG in patients with different stages of dementia under donepezil treatment may be related to different compensatory capacities due to structural and functional brain disturbances.
AN 2002:38007 HCAPLUS <<LOGINID::20080201>>
DN 136:226702
TI EEG changes during long-term treatment with donepezil in Alzheimer's disease patients
AU Kogan, E. A.; Korczyn, A. D.; Virchovsky, R. G.; Klimovizky, S. Sh.; Treves, T. A.; Neufeld, M. Y.
CS EEG and Epilepsy Unit, Tel-Aviv Sourasky Medical Center, Tel-Aviv University, Tel-Aviv, Israel
SO Journal of Neural Transmission (2001), 108(10), 1167-1173
CODEN: JNTRF3; ISSN: 1435-1463
PB Springer-Verlag Wien
DT Journal
LA English
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Ventricular measurements in computed tomography of responders and non-responders to donepezil in the treatment of Alzheimer's disease
AB INTRODUCTION: the authors attempt to see whether the ventricular measurements in routine CT scans performed prior to commencing donepezil differed in patients who duly responded well and those who did not, and to explore the potential application of the findings in clin. practice. METHOD: The study included all patients who were prescribed donepezil during a 2-yr period in Warrington (n=59). Two groups of patients were compared in respect of their baseline CT scan ventricular measurements: those who improved or remained stable cognitively on donepezil (n=43) and those who declined while on donepezil (MMSE < 10) during the study period (n=16). RESULTS: Significant differences in means between the two groups were found in relation to the bicaudate span and bicaudate ratio. Of ventricular measurements, only the bicaudate parameters were significantly correlated with the baseline Mini Mental State Examination ( MMSE) score as well as the rate of decline in cognitive function during the study period (P < 0.05). CONCLUSION: Baseline bicaudate diameter and ratio may be of some value if included in the initial assessment of patients on donepezil. These measurements, in conjunction with other cognitive and functional assessments, may prove helpful in deciding whether to commence treatment, and give a rough guide to the outcome. Future studies, with sufficient statistical power, are necessary to explore the use of ventricular parameters in predicting and monitoring patients' response to current and future pharmacol. treatment in Alzheimer's disease.
AN 2001:828000 HCAPLUS <<LOGINID::20080201>>
DN 136:128943
TI Ventricular measurements in computed tomography of responders and

non-responders to donepezil in the treatment of Alzheimer's disease
AU Salib, Emad; Sheridan, Tony; Allington, Mark
CS Hollins Park Hospital, Warrington, WA2 8WA, UK
SO International Journal of Psychiatry in Clinical Practice (2001), 5(3), 189-194
CODEN: IJPCFZ; ISSN: 1365-1501
PB Martin Dunitz Ltd.
DT Journal
LA English
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Pharmacological treatment of non-cognitive disturbances in dementia disorders
AB Behavioral and psychol. symptoms of dementia (BPSD) occur in 50-90% of patients with Alzheimer's disease (AD). They cause premature institutionalization, increased costs of care and significant loss of quality-of-life for the patient and his/her family and caregivers. Non-pharmacol. interventions are first-line in dealing with milder BPSD, while for moderate to severe BPSD, medication is clearly indicated in conjunction with non-pharmacol. interventions. An imbalance of different neurotransmitters (acetylcholine, dopamine, noradrenaline, serotonin) has been proposed as the neurochem. correlate of BPSD. An involvement of some specific brain regions responsible for emotional activities (parahippocampal gyrus, dorsal raphe, locus coeruleus) and cortical hypometabolism have been suggested to contribute to BPSD. Atypical or novel antipsychotic drugs represent the reference drugs for treating BPSD. Among these, risperidone is considered as a drug of choice. Also, selective serotonin reuptake inhibitors (SSRIs) are useful in the treatment of BPSD.
AN 2001:720167 HCAPLUS <<LOGINID::20080201>>
DN 137:57372
TI Pharmacological treatment of non-cognitive disturbances in dementia disorders
AU Parnetti, L.; Amici, S.; Lanari, A.; Gallai, V.
CS Department of Neuroscience, University of Perugia, Perugia, 06126, Italy
SO Mechanisms of Ageing and Development (2001), 122(16), 2063-2069
CODEN: MAGDA3; ISSN: 0047-6374
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Maintaining cognitive function in Alzheimer disease: how effective are current treatments?
AB A review. Cognitive impairment, a core feature of Alzheimer disease (AD), is highly correlated with functional decline and care-giver time. Over 12 mo, patients with mild-to-moderate AD deteriorate by 5-6 points from baseline on the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog). Stabilizing cognitive decline is, therefore, an important treatment outcome in AD. Cognitive deficits are thought to result in part from central cholinergic impairment, which provides the rationale for the enhancement of cholinergic neurotransmission as a treatment approach for AD. Acetylcholinesterase (AChE) inhibition has, to date, produced the most promising outcomes in clin. trials. Galantamine appears to be novel among marketed agents in that it inhibits AChE and modulates cholinergic nicotinic receptors, perhaps increasing neurotransmission via both mechanisms. Long-term effects of AChE inhibitors and galantamine on ADAS-cog scores of patients with mild-to-moderate AD have been studied in placebo controlled trials as

well as open-extension studies that followed randomized, double-blind studies for up to 6 mo. Conventional AChE inhibitors (rivastigmine and donepezil) have maintained ADAS-cog baseline scores for up to 40 wk in open extension studies, and Mini-Mental State Examination (MMSE) scores for up to 52 wk in a placebo-controlled study. The mean ADAS-cog score of galantamine-treated patients did not change from baseline at 12 mo (6 mo double-blind study followed by 6 mo open-label extension), suggesting that cognitive function had been maintained. These results suggest that cholinergic treatments, including galantamine, may stabilize cognitive decline of AD patients. This outcome is likely to make an important difference to patients and care-givers.

AN 2001:696996 HCAPLUS <<LOGINID::20080201>>
DN 136:75
TI Maintaining cognitive function in Alzheimer disease: how effective are current treatments?
AU Tariot, Pierre N.
CS Departments of Psychiatry, Medicine and Neurology, University of Rochester Medical Center, Rochester, NY, USA
SO Alzheimer Disease and Associated Disorders (2001), 15(Suppl. 1), S26-S33
CODEN: ADADE2; ISSN: 0893-0341
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease
AB Aim of this study was to investigate the efficacy and safety of donepezil in patients with moderate to severe AD (standardized Mini-Mental State Examination [sMMSE] scores of 5 to 17; Functional Assessment Staging score ≤6 at baseline). Two-hundred ninety patients were randomized to treatment in this 24-wk, double-blind, placebo-controlled trial. Patients received either donepezil 5 mg/day for the first 28 days and 10 mg/day thereafter as per the clinician's judgment (n = 144) or placebo (n = 146). The primary outcome measure was the Clinician's Interview-Based Impression of Change with caregiver input (CIBIC+). Patients' mean age was 73.6 yr (range 48 to 92 yr). Baseline demographics were similar between the treatment groups. Least squares (LS) mean ± SE sMMSE scores at baseline were 11.7 ± 0.35 for the donepezil group and 12.0 ± 0.34 for the placebo group. Patients receiving donepezil showed benefits on the CIBIC+, compared with placebo, at all visits up to week 24 ($p < 0.001$) and at week 24 last observation carried forward (LOCF) ($p < 0.0001$). All other secondary measures (including sMMSE, Severe Impairment Battery, Disability Assessment for Dementia, Functional Rating Scale, and Neuropsychiatric Inventory) showed significant differences between the groups in favor of donepezil at week 24 LOCF. Eighty-four percent of donepezil- and 86% of placebo-treated patients completed the trial. Adverse events (AE) were experienced by 83% of donepezil- and 80% of placebo-treated patients, the majority of which were rated mild in severity; 8% of donepezil- and 6% of placebo-treated patients discontinued because of AE. Laboratory and vital sign abnormalities were similar between the treatment groups. These data suggest that donepezil's benefits extend into more advanced stages of AD than those previously investigated, with very good tolerability.

AN 2001:678546 HCAPLUS <<LOGINID::20080201>>
DN 136:514
TI A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease
AU Feldman, H.; Gauthier, S.; Hecker, J.; Vellas, B.; Subbiah, P.; Whalen, E.
CS Donepezil MSAD Study Investigators Group, Division of Neurology, Clinic

for Alzheimer's Disease and Related Disorders, UBC Hospital, Vancouver, BC, V6T2B5, Can.
SO Neurology (2001), 57(4), 613-620
CODEN: NEURAI; ISSN: 0028-3878
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Cognitive deficits in Alzheimer's disease: treatment with acetylcholinesterase inhibitor agents
AB The use of acetylcholinesterase (AChe) inhibitors seems to be a promising therapeutic strategy against cognitive impairment of Alzheimer's disease (AD). We evaluated the safety and the efficacy of two AChe inhibitor agents, donepezil and rivastigmine, in the treatment of mild to moderately severe AD. Twenty-seven patients were recruited for the study. They met DSM-IV criteria for uncomplicated AD and NINCDS-ADRDA criteria for probable or possible AD of mild to moderate severity. Mini mental state examination (MMSE) scores of 10-21 at screening were required. Patients' age was between 53-77 yr. Sixteen patients were treated with donepezil, 5 mg/day, and 11 subjects received rivastigmine, 6-9 mg/day for 30 wk. The rating instruments used were the MMSE , the cognitive subscale of the AD assessment scale (ADAS-Cog), and the phys. self-maintenance scale (PSMS). The assessment was carried out at baseline and at weeks 6, 12, 18, 24, and 30. The results demonstrated the pos. effects of these agents on the cognitive and functional pictures in patients with mild to moderately severe AD. The adverse events related to treatment were generally not troublesome, and were of short duration (nausea, vomiting, dizziness, and diarrhea).
AN 2001:633476 HCAPLUS <<LOGINID::20080201>>
DN 135:352692
TI Cognitive deficits in Alzheimer's disease: treatment with acetylcholinesterase inhibitor agents
AU Fuschillo, C.; La Pia, S.; Campana, F.; Pinto, A.; De Simone, L.
CS Department of Mental Health, Neuropsychogeriatric Ward of Pollena Trocchia, Pollena Trocchia (Napoli), I-80040, Italy
SO Archives of Gerontology and Geriatrics, Supplement (2001), 7(Cognitive, Affective and Behavior Disorders in the Elderly), 151-158
CODEN: AGGSEU; ISSN: 0924-7947
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Chronic donepezil treatment is associated with slowed cognitive decline in Alzheimer's disease
AB A decline in cognition was compared between probable Alzheimer's disease (AD) patients treated with long-duration cholinesterase inhibitors (ChE-Is) and those who remained untreated. ChE-Is, including donepezil and tacrine, have shown beneficial effects on cognition and global functioning in patients with AD. The duration of these benefits is unknown because the longest double-blind placebo-controlled studies reported were only approx. 6 mo long. Ethical concerns regarding randomization of patients to placebo for long periods make it difficult to undertake trials of longer duration. We identified patients in 4 AD centers who were or were not consistently treated with ChE-Is and who had demog., psychometric and follow-up data. We compared 205 ChE-I-treated and 218 untreated AD patients on baseline variables hypothesized to differ between these groups, on baseline Mini Mental Status Examination (MMSE ) scores and on rates of MMSE change at 1 yr. The anal. was

performed initially with all ChE-I-treated patients as a single group vs. untreated subjects, and then with donepezil vs. untreated subjects and tacrine vs. untreated subjects. As expected, treated and untreated patients differed with respect to age, education, ethnicity, percentage of community dwelling and exact days of follow-up (ANOVA and X2) in several comparisons, but did not differ on baseline MMSE score. These baseline variables were highly intercorrelated. MMSE scores declined significantly more slowly after 1 yr of ChE-I treatment compared to untreated patients ($p = 0.05$) after controlling for baseline differences in age, education, ethnicity and percentage of community dwelling. Slowing of decline was significant in the donepezil-treated patients ($p = 0.007$) but not in the tacrine-treated group ($p = 0.33$). This study, utilizing concurrent, nonrandomized controls, suggests that donepezil continues to have efficacy over at least the first year of therapy. Other studies are needed to determine whether the benefits are maintained beyond 1 yr.

AN 2001:452614 HCAPLUS <<LOGINID::20080201>>
DN 135:267106
TI Chronic donepezil treatment is associated with slowed cognitive decline in Alzheimer's disease
AU Doody, R. S.; Dunn, J. K.; Clark, C. M.; Farlow, M.; Foster, N. L.; Liao, T.; Gonzales, N.; Lai, E.; Massman, P.
CS Baylor College of Medicine Alzheimer's Disease Research Center (AGO-8664), Houston, TX, 77030-3498, USA
SO Dementia and Geriatric Cognitive Disorders (2001), 12(4), 295-300
CODEN: DGCDFX; ISSN: 1420-8008
PB S. Karger AG
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Efficacy of acetylcholinesterase inhibitors versus nootropics in Alzheimer's disease: A retrospective, longitudinal study
AB The aim of this study was to investigate the efficacy of nootropics (piracetam, aniracetam, nimodipine and dihydroergocristine) vs. acetylcholinesterase inhibitors (AChE-Is) (tacrine and donepezil) in the treatment of Alzheimer's disease. This is a retrospective study of 510 patients with Alzheimer's disease. To determine clin. efficacy of treatment, we used the mean change over time in scores for the following tests: the Mini-Mental State Examination (MMSE); the Cambridge Cognitive Examination for the Elderly; and the Functional Rating Scale for Symptoms of Dementia. In all patients and in patients with severe Alzheimer's disease (baseline MMSE < 11), no significant differences were seen in the neuropsychol. test scores between the two treatment groups. In patients with moderate dementia (baseline MMSE between 11 and 20), however, there was a significantly greater deterioration, as shown on the CAMCOG scale, after 12 mo' treatment for patients receiving AChE-Is compared with those receiving nootropics (-4.38 for AChE-Is group vs. 1.48 for nootropics group). For patients with mild dementia (baseline MMSE score between 21 and 26), there was a significantly greater deterioration on the MMSE scale for each time-point in the nootropics group compared with the AChE-Is group. In conclusion, we did not find any strong evidence that a difference in efficacy exists between AChE-Is and nootropics in the treatment of Alzheimer's disease.
AN 2001:246165 HCAPLUS <<LOGINID::20080201>>
DN 135:190250
TI Efficacy of acetylcholinesterase inhibitors versus nootropics in Alzheimer's disease: A retrospective, longitudinal study
AU Tsolaki, M.; Pantazi, T.; Kazis, A.
CS Third Department of Neurology, Aristotle University of Thessaloniki,

Thessaloniki, Greece
SO Journal of International Medical Research (2001), 29(1), 28-36
CODEN: JIMRBV; ISSN: 0300-0605
PB Cambridge Medical Publications Ltd.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil, rivastigmine, and vitamin E in Alzheimer disease: a combined P300 event-related potentials/neuropsychologic evaluation over 6 months
AB The latency of P300 "cognitive" event-related potentials changes if cholinergic activities of the central nervous system are pharmacol. manipulated. We tested the hypothesis that the new cholinesterase inhibitors donepezil (DPZ) and rivastigmine (Riv) may have an effect on the frequently abnormal P300 component in patients with Alzheimer disease (AD), thereby allowing a significant evaluation of cholinesterase inhibitors. We evaluated 60 patients with mild to moderately severe probable AD, in comparison with 60 age-matched control subjects, with P300 recordings and neuropsychol. examns. Forty patients were randomly assigned in a double-blinded trial to 5-10 mg/d DPZ vs. 2,000 IU/d vitamin E, and 20 patients were instead treated in an open trial with 1.5 to 12 mg/d Riv. In patients treated with vitamin E, we observed latency increments (7.4±3.5 ms) correlated with worsening neuropsychol. test scores. In patients treated with DPZ and Riv, we found significant P300 latency redns. (15.3±3.2 ms and 22.0±3.3 ms). Shorter P300 latencies were associated with higher Wechsler Adult Intelligence Scale scores and with lower AD Assessment Scale-cognitive subscale (ADAS-cog) scores (R = 0.72). Correlations between ADAS-cog changes and P300 changes significantly separated patients treated with DPZ and Riv from those treated with vitamin E. Administration of DPZ and Riv reduced the latencies of P300 components proportionately to neuropsychol. test improvements. Combined P300 and neuropsychol. test evaluation significantly separated DPZ-treated patients and Riv-treated patients from vitamin E-treated patients.
AN 2001:224013 HCAPLUS <<LOGINID::20080201>>
DN 135:175156
TI Donepezil, rivastigmine, and vitamin E in Alzheimer disease: a combined P300 event-related potentials/neuropsychologic evaluation over 6 months
AU Thomas, Astrid; Iacono, Diego; Bonanni, Laura; D'Andreamatteo, Giordano; Onofrj, Marco
CS Department of Oncology and Neuroscience, Institute of Neurophysiopathology, University "G. D'Annunzio", Pescara, Italy
SO Clinical Neuropharmacology (2001), 24(1), 31-42
CODEN: CLNEDB; ISSN: 0362-5664
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil dose-dependently inhibits acetylcholinesterase activity in various areas and in the presynaptic cholinergic and the postsynaptic cholinoceptive enzyme-positive structures in the human and rat brain
AB In the symptomatic treatment of mild to moderately severe dementia associated with Alzheimer's disease, donepezil (E2020) has been introduced for the inhibition of acetylcholinesterase activity in the human brain. However, there is no morphol. evidence as to how this chemical agent affects the acetylcholinesterase-pos. structures in the various areas of the human and the rat CNS. This study demonstrates by histochem.

means that donepezil exerts a dose-dependent inhibitory effect in vitro on acetylcholinesterase activity. The most sensitive areas were the cortex and the hippocampal formation. Within the different layers of the cortex, the cholinoceptive acetylcholinesterase-pos. postsynaptic pyramidal cell bodies were more sensitive than the presynaptic cholinergic axonal processes. In the cortex, the cell body staining was already abolished by even 2 + 10-8 M donepezil, whereas the axonal staining could be eliminated only by at least 5 + 10-8 M donepezil. In the hippocampus, the axonal acetylcholinesterase reaction end-product was eliminated by 5 + 10-7 M donepezil. The most resistant region was the putamen, where the staining intensity was moderately reduced by 1 + 10-6 M donepezil. In the rat brain, the postsynaptic cholinoceptive and presynaptic cholinergic structures were inhibited by nearly the same dose of donepezil as in the human brain. These histochem. results provide the first morphol. evidence that, under in vitro circumstances, donepezil is not a general acetylcholinesterase inhibitor in the CNS, but rather selectively affects the different brain areas and, within these, the cholinoceptive and cholinergic structures. The acetylcholinesterase staining in the nerve fibers (innervating the intracerebral blood vessels of the human brain and the extracerebral blood vessels of the rat brain) and at the neuromuscular junction in the diaphragm and gastrocnemius muscle of rat, was also inhibited dose dependently by donepezil. It is concluded that donepezil may be a valuable tool with which to influence both the pre- and the postsynaptic acetylcholinesterase-pos. structures in the human and rat central and peripheral nervous systems.

AN 2000:856528 HCAPLUS <<LOGINID::20080201>>
DN 134:110396
TI Donepezil dose-dependently inhibits acetylcholinesterase activity in various areas and in the presynaptic cholinergic and the postsynaptic cholinoceptive enzyme-positive structures in the human and rat brain
AU Kasa, P.; Papp, H.; Kasa, P., Jr.; Torok, I.
CS Alzheimer's Disease Research Centre, University of Szeged, Szeged, H-6720, Hung.
SO Neuroscience (Oxford) (2000), 101(1), 89-100
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Effects of donepezil on emotional/behavioral symptoms in Alzheimer 's disease patients
AB This open-label study examined the effects of the reversible cholinesterase inhibitor donepezil on emotional/behavioral symptoms in Alzheimer 's disease (AD) patients. Patients were diagnosed as having probable/possible AD by National Institute of Neurol. and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria. This study used the CERAD Behavior Rating Scale for Dementia (CBRSD) and its subscales to evaluate a group of 25 AD patients treated with donepezil. Dosage was increased at 4 mo for most patients from 5 to 10 mg q.h.s. Anal. of variance was used to compare scores over a period of 12 mo. These patients were also compared, using t tests, to a reference group that had received no donepezil or other anticholinesterase. Donepezil administration was associated with improvement in Mini-Mental State Examination (MMSE) and CBRSD total scores at 3-mo evaluation ($p \leq .05$). CBRSD depression and behavioral dysregulation scores improved transiently at 4 mo ($p \leq .05$). MMSE, CBRSD total, CBRSD depression, and CBRSD behavioral dysregulation scores returned to baseline levels at 12 mo, in contrast to the reference group, whose MMSE and CBRSD total scores worsened minimally over the 12 mo. Donepezil has a mildly pos. effect on

emotional/behavioral symptoms in AD in addition to its effect on cognitive function.
AN 2000:574998 HCAPLUS <<LOGINID::20080201>>
DN 133:359113
TI Effects of donepezil on emotional/behavioral symptoms in Alzheimer 's disease patients
AU Weiner, Myron F.; Martin-Cook, Kristin; Foster, Barbara M.; Saine, Kathleen; Fontaine, Catherine S.; Svetlik, Doris A.
CS Departments of Psychiatry and Neurology, University of Texas Southwestern Medical Center, Dallas, TX, 75235-9070, USA
SO Journal of Clinical Psychiatry (2000), 61(7), 487-492
CODEN: JCLPDE; ISSN: 0160-6689
PB Physicians Postgraduate Press, Inc.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicenter open-label study
AB This multicenter, open-label study evaluated the long-term efficacy and safety of donepezil in the treatment of patients with mild to moderately severe Alzheimer's disease (AD). The 133 patients who entered the study had previously completed a 14-wk randomized, double-blind, placebo-controlled study with donepezil. In this open-label study, patients were treated initially with 3 mg per day donepezil, which could be increased to 5, 7 and 10 mg per day in a step-wise fashion. Patients attended the clinic for assessments at 3-wk intervals for the first 12 wk, then subsequently at 12-wk intervals for up to 240 wk (254 cumulative weeks). Efficacy was assessed using the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) and the Clin. Dementia Rating-Sum of the Boxes scale (CDR-SB), and data were compared with those predicted for historical untreated AD patients. During the first 6-9 mo of the study, mean ADAS-cog and CDR-SB scores showed evidence of clin. improvement from baseline. After this time scores gradually deteriorated. Overall the decline was less than that estimated if this cohort of patients had not been treated. The most common adverse events were related to the nervous and digestive systems, and were generally mild and transient, resolving without the need for dose modifications. There was no evidence of hepatotoxicity. In conclusion, these data demonstrate that donepezil is a well-tolerated, realistic symptomatic treatment for AD over a period of up to 4.9 yr. An interim report of the first 98 wk of the study has been published previously.
AN 2000:285344 HCAPLUS <<LOGINID::20080201>>
DN 133:114939
TI Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicenter open-label study
AU Rogers, S. L.; Doody, R. S.; Pratt, R. D.; Ieni, J. R.
CS Eisai Co. Ltd., Tokyo, Japan
SO European Neuropsychopharmacology (2000), 10(3), 195-203
CODEN: EURNE8; ISSN: 0924-977X
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A comparative study in rats of the in vitro and in vivo pharmacology of the acetylcholinesterase inhibitors tacrine, donepezil and NXX-066
AB The in vitro and in vivo effects of the novel acetylcholinesterase

inhibitors donepezil and NXX-066 have been compared to tacrine. Using purified acetylcholinesterase from elec. eel both tacrine and donepezil were shown to be reversible mixed type inhibitors, binding to a similar site on the enzyme. In contrast, NXX-066 was an irreversible non-competitive inhibitor. All three compds. were potent inhibitors of rat brain acetylcholinesterase (IC50 [nM]; tacrine: 125; NXX-066: 148; donepezil: 33). Tacrine was also a potent butyrylcholinesterase inhibitor. Donepezil and tacrine displaced [3H]pirenzepine binding in rat brain homogenates (IC50 values [μM]; tacrine: 0.7; donepezil: 0.5) but NXX-066 was around 80 times less potent at this M1-muscarinic site. Studies of carbachol stimulated increases in [Ca2+]i in neuroblastoma cells demonstrated that both donepezil and tacrine were M1 antagonists. Ligand binding suggested little activity of likely pharmacol. significance with any of the drugs at other neurotransmitter sites. I.p. administration of the compds. to rats produced dose dependent increases in salivation and tremor (ED50 [μmol/kg]; tacrine: 15, NXX-066: 35, donepezil: 6) with NXX-066 having the most sustained effect on tremor. Following oral administration, NXX-066 had the slowest onset but the greatest duration of action. The relative potency also changed, tacrine having low potency (ED50 [μmol/kg]; tacrine: 200, NXX-066: 30, donepezil: 50). Salivation was severe only in tacrine treated animals. Using in vivo microdialysis in cerebral cortex, both NXX-066 and tacrine were found to produce a marked (at least 30-fold) increase in extracellular acetylcholine which remained elevated for more than 2 h after tacrine and 4 h after NXX-066. The results are discussed in relation to the treatment of Alzheimer's disease with acetylcholinesterase inhibitors.

AN 1999:159251 HCAPLUS <<LOGINID::20080201>>
DN 130:332723
TI A comparative study in rats of the in vitro and in vivo pharmacology of the acetylcholinesterase inhibitors tacrine, donepezil and NXX-066
AU Snape, M. F.; Misra, A.; Murray, T. K.; De Souza, R. J.; Williams, J. L.; Cross, A. J.; Green, A. R.
CS Astra Neuroscience Research Unit, London, WC1N 1PJ, UK
SO Neuropharmacology (1999), 38(1), 181-193
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Perspectives in the management of Alzheimer's disease: clinical profile of donepezil
AB A review with 66 refs. Donepezil-HCl is a piperidine-based reversible acetylcholinesterase (AChE) inhibitor, chemical distinct from other cholinesterase inhibitors and rationally designed to treat the symptoms of Alzheimer's disease (AD). It is highly selective for AChE in the central nervous system (CNS), with little or no affinity for butyrylcholinesterase. In preclin. studies in animals, donepezil produced increased CNS acetylcholine. The resultant enhancement of cholinergic activity gave rise to improved performance by rats on tests of learning and memory, with no evidence of hepatic or renal toxicity. In subsequent phase I clin. evaluations in healthy volunteers, donepezil demonstrated favorable pharmacokinetic, pharmacodynamic and safety profiles. Its long terminal disposition half-life supported once-daily administration, with no requirement for dose modification in the elderly or in patients with renal or hepatic impairment. A 14-wk, phase II dose-finding study in patients with mild to moderate AD (Clin. Dementia Rating, 1-2; Mini-Mental State Examination [MMSE], 10-26) showed that donepezil at 5 mg/day produced highly significant improvements in cognition (as measured by the Alzheimer's Disease Assessment Scale, cognitive subscale [ADAS-cog]). Subsequently, 2 pivotal parallel-group, placebo-controlled

phase III trials (of 15- and 30-wk duration) showed highly significant improvements in ADAS-cog, MMSE, Clinician's Interview-Based Impression of Change with caregiver input and CDR-SB (Sum of the Boxes) scores, compared with placebo, in mild to moderate AD patients treated with either 5 or 10 mg donepezil/day. Adverse events in the phase II and III trials were mild and transient and resolved with continued donepezil administration. The donepezil clin. trials program has shown that this drug is a clin. effective and well-tolerated once-daily treatment for the symptoms of mild to moderate AD.

AN 1998:761693 HCAPLUS <<LOGINID::20080201>>
DN 130:162621
TI Perspectives in the management of Alzheimer's disease: clinical profile of donepezil
AU Rogers, S. L.
CS Eisai Co Ltd, Tokyo, Japan
SO Dementia and Geriatric Cognitive Disorders (1998), 9(Suppl. 3), 29-42
CODEN: DGCDFX; ISSN: 1420-8008
PB S. Karger AG
DT Journal; General Review
LA English
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study
AB Donepezil hydrochloride (Aricept) is a selective acetylcholinesterase inhibitor developed for the treatment of Alzheimer disease. This phase 3 study was 1 of 2 pivotal trials undertaken to establish the efficacy and safety of using donepezil in patients with mild to moderately severe Alzheimer disease. Objectives were to further examine the efficacy and safety of using donepezil in the treatment of patients with mild to moderately severe Alzheimer disease. In addition, this study examined the relationships between plasma donepezil concns., inhibition of red blood cell acetylcholinesterase activity, and clin. response. This was a 12-wk, double-blind, placebo-controlled, parallel-group trial with a 3-wk single-blind washout. Outpatients at 23 centers in the United States were randomized to receive placebo, 5 mg of donepezil hydrochloride, or 10 mg of donepezil hydrochloride (5 mg/d during week 1 then 10 mg/d thereafter) administered once daily at bedtime. Primary efficacy was measured using the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-cog) and Clinician's Interview-Based Impression of Change including care-giver information (CIBIC plus). A total of 468 patients entered the study, more than 97% of whom were included in the intention-to-treat (end point) analyses. The use of donepezil produced statistically significant improvements in ADAS-cog, CIBIC plus, and Mini-Mental State Examination scores, relative to placebo. The mean drug-placebo differences, at end point, for the groups receiving 5 mg/d and 10 mg/d of donepezil hydrochloride were, resp., 2.5 and 3.1 units for ADAS-cog ($P<.001$); 0.3 and 0.4 units for CIBIC plus ($P\leq.008$); and 1.0 and 1.3 units for Mini-Mental State Examination ($P\leq.004$). On the CIBIC plus scale, 32% and 38% of patients, resp., treated with 5 mg/d and 10 mg/d of donepezil hydrochloride demonstrated clin. improvement (a score of 1, 2, or 3) compared with placebo (18%). The mean ($\pm$ SEM) donepezil plasma concns. at study end point were 25.9 $\pm$ 0.7 ng/mL and 50.6 $\pm$ 1.9 ng/mL in the groups receiving dosages of 5 mg/d and 10 mg/d, resp. Corresponding mean ($\pm$ SEM) percentages of inhibition of red blood cell acetylcholinesterase activity were 63.9% $\pm$ 0.9% and 74.7% $\pm$ 1.2% for these 2 dosages, resp. There was a statistically significant pos. correlation between plasma concns. of donepezil and acetylcholinesterase inhibition; the EC50 (50% effect) was obtained at a concentration of 15.6 ng/mL. A plateau of inhibition (80%-90%) was reached at plasma donepezil concns. higher than

50 ng/mL. The correlations between plasma drug concns. and both ADAS-cog (P<.001) and CIBIC plus (P =.006) were also statistically significant, as were the correlations between red blood cell acetylcholinesterase inhibition and change in ADAS-cog (P<.001) and CIBIC plus (P =.005). The incidence of treatment-emergent adverse events with both dosages of donepezil (68%-78%) was comparable with that observed with placebo (69%). The use of 10 mg/d of donepezil hydrochloride was associated with transient mild nausea, insomnia, and diarrhea. There were no treatment-emergent clin. significant changes in vital signs or clin. laboratory test results. More important, the use of donepezil was not associated with the hepatotoxic effects observed with acridine-based cholinesterase inhibitors. Donepezil hydrochloride (5 and 10 mg) administered once daily is a well-tolerated and efficacious agent for treating the symptoms of mild to moderately severe Alzheimer disease.

AN 1998:328223 HCAPLUS <<LOGINID::20080201>>
DN 129:62869
TI Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study
AU Rogers, Sharon L.; Doody, Rachelle S.; Mohs, Richard C.; Friedhoff, Lawrence T.; Alter, Milton; Apter, Jeffrey; Williams, Troy; Baumel, Barry; Brown, Walter; Clark, Christopher; Cohan, Stanley; Farlow, Martin; Farmer, Mildred; Folks, David; Geldmacher, David; Heiser, Jon; Jurkowski, Claire; Krishnan, K. Ranga; Pelchat, Rodney; Sadowsky, Carl; Sano, Mary; Strauss, Abbey; Tune, Larry; Webster, James; Weiner, Myron; Stark, Stuart
CS Eisai Inc., Teaneck, NJ, USA
SO Archives of Internal Medicine (1998), 158(9), 1021-1031
CODEN: AIMDAP; ISSN: 0003-9926
PB American Medical Association
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease
AB The efficacy and safety of donepezil as a treatment for patients with mild to moderate Alzheimer's disease (AD) was investigated in a multicenter, double-blind study. Patients were randomly assigned to treatment with placebo, 5 mg/d donepezil, or 10 mg/d donepezil for 24 wk followed by a 6-wk, single-blind placebo washout. The primary efficacy measures were the cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-cog) and the Clinician's Interview Based Assessment of Change-Plus (CIBIC plus), with the Mini-Mental State Examination ( MMSE), Clin. Dementia Rating Scale-Sum of the Boxes (CDR-SB), and patient rated Quality of Life (QoL) used as secondary measures. Cognitive function, as measured by the ADAS-cog, was improved in the 5- and 10-mg/d donepezil groups as compared with the placebo group at weeks 12, 18, and 24. Clinician's global ratings on the CIBIC plus also improved in both the 5- and 10-mg/d donepezil groups relative to placebo. At the end of the 6-wk placebo washout phase, ADAS-cog scores and CIBIC plus ratings were not different for the three groups. Significant treatment benefits were also observed consistently in both the 5- and 10-mg/d groups on the MMSE and the CDR-SB, but there was no consistent effect on the patient-rated QoL. Cholinergic side effects (primarily diarrhea, nausea, and vomiting) were reported more often in the 10-mg/d group than either the 5-mg/d or placebo groups. Side effects were transient and generally mild in severity. Thus, that donepezil is a well-tolerated drug that improves cognition and global function in patients with mild to moderate AD.

AN 1998:80602 HCAPLUS <<LOGINID::20080201>>
DN 128:213228
TI A 24-week, double-blind, placebo-controlled trial of donepezil in patients

with Alzheimer's disease
AU Rogers, S. L.; Farlow, M. R.; Doody, R. S.; Mohs, R.; Friedhoff, L. T.; Donepezil Study Group
CS Eisai Inc., Teaneck, NJ, USA
SO Neurology (1998), 50(1), 136-145
CODEN: NEURAI; ISSN: 0028-3878
PB Lippincott-Raven Publishers
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Donepezil (E2020): a new acetylcholinesterase inhibitor. Review of its pharmacology, pharmacokinetics, and utility in the treatment of Alzheimer's disease
AB A review, with 44 refs. Donepezil is an acetylcholinesterase inhibitor under development for the treatment of mild-moderately severe Alzheimer's disease. In vitro, donepezil is about 10 times more potent than tacrine as an inhibitor of acetylcholinesterase. Donepezil is 500- to 1000-fold selective for acetylcholinesterase over butyrylcholinesterase. In animal models, donepezil produces pos. effects on both working memory and long-term memory. In man, donepezil is slowly absorbed from the gastrointestinal (GI) tract. The compound has a terminal elimination half-life of 50 - 70 h in young volunteers; in elderly volunteers, the half-life of the compound is extended to over 100 h. Donepezil is extensively metabolized after oral administration. The parent compound is 93% bound to plasma proteins. Results from two clin. trials with donepezil have been published. The largest of these trials was a 12 wk 161 patient Phase II investigation in the USA. Results from this investigation showed that donepezil produced dose-related improvements, with statistically significant effects occurring at doses of 3 and 5 mg/day. The results published to date suggest that donepezil will be a useful agent in the symptomatic treatment of Alzheimer's disease.
AN 1997:706783 HCAPLUS <<LOGINID::20080201>>
DN 128:18286
TI Donepezil (E2020): a new acetylcholinesterase inhibitor. Review of its pharmacology, pharmacokinetics, and utility in the treatment of Alzheimer's disease
AU Heydorn, William E.
CS Synaptic Pharmaceutical Corporation, Paramus, NJ, 07652, USA
SO Expert Opinion on Investigational Drugs (1997), 6(10), 1527-1535
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT